

REMARKS

Claims 23-41 are pending, upon entry of the amendment submitted above. Favorable reconsideration is respectfully requested.

Rejection under 35 U.S.C. 112

Claims 1-3, 6, 8-11, and 17-22 were rejected under 35 U.S.C. 112, second paragraph, as indefinite. This rejection is rendered moot by cancellation of these claims. In addition, the newly-added claims specify a patient. Accordingly, withdrawal of this ground of rejection is respectfully requested.

Interference with U.S. Patent No. 6,379,708 to Howell, et al.

As discussed with the examiner, it is believed this application should be placed in an interference with U.S. Patent No. 6,379,708 to Howell et al. (hereinafter referred to as "the Howell et al. patent"). To facilitate declaration of an interference, claims 1-22 have been cancelled and replaced with new claims 23-41.

A Suggestion for an Interference with the Howell et al. patent is submitted herewith.

Please note that Supplemental Information Disclosure Statements were filed on April 28, 2005 and February 11, 2005, to cite additional prior art that was considered during the prosecution of the Howell et al. patent.

Priority Claim

The priority of this application was amended January 22, 2003, to claim priority to U.S.S.N. 09/699,003 filed October 26, 2000, which is a continuation of U.S.S.N. 09/316,226 filed May 21, 1999, now U.S. Patent No. 6,231,536, which claims priority to U.S.S.N. 09/083,307 filed May 22, 1998, and to U.S.S.N. 60/164,695 filed November 10, 1999.

Application No. 09/709,045
Reply to Office Action of January 10, 2005

Although the examiner has not requested an amended declaration of inventorship, applicant is submitting under separate cover a substitute declaration explicitly claiming priority to the earlier applications.

Please contact the undersigned by telephone if anything further is required.

Respectfully submitted,

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DOCKET NO: LEN 102

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF :
M. RIGDON LENTZ : EXAMINER: L. SPECTOR
SERIAL NO: 09/709,045 :
FILED: NOVEMBER 10, 2000 : GROUP ART UNIT: 1647
FOR: METHOD AND SYSTEM TO :
REMOVE CYTOKINE INHIBITOR IN
PATIENTS

37 CFR 41.202 SUGGESTION OF AN INTERFERENCE

COMMISSIONER FOR PATENTS
ALEXANDRIA, VIRGINIA 22313

SIR:

37 CFR 41.202(a)(1)

The applicant seeks an interference between the present application and U.S. patent No. 6,379,708, naming Howell et al. as inventors (hereinafter referred to as "the Howell et al. patent"). For the Examiner's convenience, a copy of the Howell et al. patent is submitted herewith.

37 CFR 41.202(a)(2)

Applicant believes that its claims 23-41 interfere with claims 1-44 of the Howell et al. patent.

Applicant proposes the following count:

Claim 23 of the present application

or

Claim 1 of the Howell et al. patent.

Applicant's claims 23-41 should be designated as corresponding to the proposed count. Claim 23 corresponds because it is literally one-half of the proposed count. Claims 24-41 each depend from claim 23 and specify narrower embodiments of the invention which are currently asserted to be not patentably distinct from claim 23.

Claims 1-44 of the Howell et al. patent should be designated as corresponding to the proposed count. Claim 1 corresponds because it is literally one-half of the proposed count.

Claims 2-44 of the Howell et al. patent are directed to the same patentable invention as the proposed count. The comments below refer to the claims of the Howell et al. patent.

The field of the invention defined by the claims of the present application and the Howell et al. patent is, generally speaking, blood filtration-- i.e., removing a component from blood. The relevant timeframe is just prior to May 22, 1998. As will be discussed below, that date is the earliest date to which applicant claims benefit under 35 USC §120.

Howell's claim 2 specifies that the binding partner is attached to an inert medium to form an absorbent matrix. Claim 24 of the present application specifies that the cytokine receptor inhibitor is immobilized in a solid support or membrane. Those claims are directed to the same patentable invention since a solid support or membrane is a well-known example of an adsorbent matrix. Since claim 24 of the present application corresponds to the proposed count for the reasons discussed above, Howell's claim 2 corresponds for the same reasons.

Howell's claim 3 specifies that the binding partner is covalently joined to the inert medium. Covalently attaching a binding partner to an inert medium was well-known in the relevant timeframe. In addition, it was widely appreciated that covalent attached is generally robust as compared to non-covalent attachment, because non-covalent attachments are much easier to disrupt by, for example, an increase in temperature or a change in solution conditions (i.e., increasing the salt concentration). Therefore, Howell's claim 3 corresponds to the proposed count.

Howell's claims 4-9 recite specific types of inert media. Howell et al. state that such media are well-known in the relevant field. See the Howell et al. patent at column 8, lines 35-40.

Howell's claim 10 specifies that the binding partner is a binding partner to which the targeted immune system inhibitor binds in nature. This corresponds to the "cytokine molecules" specified as a selection for the "cytokine receptor inhibitor" in (c) of claim 23 of the present application. Cytokines bind in nature to the soluble cytokine receptors in nature. Since claim 1 of the present application corresponds to the proposed count for the reasons discussed above, Howell's claim 10 corresponds as well.

Howell's claim 11 specifies that the binding partner is made recombinantly. It was well-known in the relevant timeframe that products such as cytokines could be made recombinantly. Therefore, Howell's claim 11 corresponds to the proposed count.

Howell's claim 12 specifies that the binding partner is a fragment of a binding partner to which the targeted immune system inhibitor binds in nature. This corresponds to the epitopes of cytokine molecules specified as a selection for the "cytokine receptor inhibitor" in (c) of claim 23 of the present application. Cytokines bind in nature to the soluble cytokine receptors in nature. Since claim 1 of the present application corresponds to the proposed count for the reasons discussed above, Howell's claim 12 corresponds as well.

Howell's claim 13 specifies that the fragment is made recombinantly. It was well-known in the relevant timeframe that products such as cytokine fragments could be made recombinantly. Therefore, Howell's claim 13 corresponds to the proposed count.

Howell's claim 14 specifies that the binding partner is a monoclonal antibody. Claim 36 of the present application specifies a monoclonal antibody. Since claim 36 of the present application corresponds to the proposed count for the reasons discussed above, Howell's claim 14 corresponds for the same reasons.

Howell's claim 15 specifies that the monoclonal antibody is produced recombinantly. Claim 38 of the present application specifies a recombinant monoclonal antibody. Since claim 38 of the present application corresponds to the proposed count for the reasons discussed above, Howell's claim 15 corresponds for the same reasons.

Howell's claim 16 specifies that the binding partner is a fragment of a monoclonal antibody. Claim 36 of the present application specifies a monoclonal antibody fragment. Since claim 36 of the present application corresponds to the proposed count for the reasons discussed above, Howell's claim 16 corresponds for the same reasons.

Howell's claim 17 specifies that the monoclonal antibody fragment is produced recombinantly. Claim 38 of the present application specifies a recombinant monoclonal antibody fragment. Since claim 38 of the present application corresponds to the proposed count for the reasons discussed above, Howell's claim 17 corresponds for the same reasons.

Howell's claims 18, 20, 24, and 25 specify a mixture of antibodies or fragments. Claim 26 of the present application specifies a mixture of antibodies. Since claim 26 of the present application corresponds to the proposed count for the reasons discussed above, Howell's claims 18, 20, 24, and 25 correspond for the same reasons.

Howell's claims 19 and 21 specify that the antibodies or fragments are produced recombinantly. Claim 25 of the present application specifies recombinant antibodies. Since claim 25 of the present application corresponds to the proposed count for the reasons discussed above, Howell's claims 19 and 21 correspond for the same reasons.

Howell's claims 22 and 23 specify a polyclonal antibody preparation or fragments of a polyclonal antibody preparation. Claim 35 of the present application specifies polyclonal antibodies or fragments. Since claim 35 of the present application corresponds to the proposed count for the reasons discussed above, Howell's claims 22 and 23 correspond for the same reasons.

Howell's claims 26-31 are each directed to an embodiment in which the binding peptide is a synthetic peptide. Claim 23 of the present application specifies epitopes of cytokine molecules specified as a selection for the "cytokine receptor inhibitor" in (c). An epitope of a cytokine is a fragment of a cytokine which is capable of binding to the cytokine receptor inhibitor. Cytokines are peptides. Therefore, an epitope of a cytokine is also a peptide. Synthesizing peptides was well-known in the relevant field in the relevant timeframe. For these reasons, Howell's claims 26-31 correspond to the proposed count.

Howell's claim 32 specifies that steps (a) through (e) are repeated. Claim 41 of the present application specifies repeating steps (a)-(e). Since claim 41 corresponds to the proposed count for the reasons discussed above, Howell's claim 32 also corresponds for the same reason.

Howell's claim 33 specifies that the mammal is a human. Claim 27 of the present application specifies that the patient is a human. Since claim 27 of the present application corresponds to the proposed count for the reasons discussed above, Howell's claim 33 also corresponds for the same reason.

Howell's claim 34 specifies that the mammal is a non-human. Claim 23 of the present application specifies "a patient." A non-human mammal is a sufficiently large genus such that it is not patentably distinct from "a patient." Therefore, Howell's claim 34 corresponds to the proposed count.

Howell's claims 35 and 36 specify that the binding partner bound to the targeted immune system inhibitor is removed by mechanical means or chemical/biological means, respectively. Claim 23 of the present application specifies a group of cytokine receptor inhibitors, all of which are chemical compounds. In addition, claim 24 of the present application specifies that the cytokine receptor inhibitor is immobilized on a solid support or membrane, which is a mechanical means of performing the separation. See column 8, lines

47-55 of the Howell et al. patent. Since claims 23 and 24 of the present application correspond to the proposed count for the reasons discussed above, Howell's claim 35 also corresponds.

Howell's claim 37 is an independent claim. That claim is directed to the same general method as claim 1 of that patent but is narrower by specifying an antibody, attached to an inert medium. Claim 23 of the present application specifies an antibody, and claim 24 specifies that the antibody is immobilized in a solid support or membrane. Thus, the subject matter of those claims is directed to the same patentable invention as Howell's claim 37. Since claims 23 and 24 of the present application correspond to the proposed count for the reasons discussed above, Howell's claim 37 also corresponds.

Howell's claim 38 is an independent claim. That claim is directed to the same general method as claim 1 of the Howell et al. patent but is narrower by specifying an antibody that specifically binds to soluble receptors for tumor necrosis factors α and β . Claim 28 of the present application specifies the soluble cytokine receptor is selected from the group consisting of soluble receptors for tumor necrosis factors alpha and beta. Since claim 28 of the present application correspond to the proposed count for the reasons discussed above, Howell's claim 38 also corresponds.

Howell's claim 39 specifies that at least one antibody is attached to an inert medium to form an absorbent matrix. Claim 24 of the present application specifies that the cytokine receptor inhibitor is immobilized on a solid support or membrane. Those claims are directed to the same patentable invention since a solid support or membrane is a well-known example of an adsorbent matrix. Since claim 24 of the present application corresponds to the proposed count for the reasons discussed above, Howell's claim 39 corresponds for the same reasons.

Howell's claim 40 specifies that at least one antibody is covalently joined to the inert medium. Covalently attaching a binding partner to an inert medium was well-known in the

relevant timeframe. In addition, it was widely appreciated that a covalent attachment is generally robust as compared to non-covalent attachment, because non-covalent attachments are much easier to disrupt by, for example, an increase in temperature or a change in solution conditions (i.e., increasing the salt concentration). Therefore, Howell's claim 40 corresponds to the proposed count.

Howell's claim 41 specifies that the at least one antibody is a monoclonal antibody or a fragment of a monoclonal antibody. Claim 36 of the present application specifies a monoclonal antibody. Since claim 36 of the present application corresponds to the proposed count for the reasons discussed above, Howell's claim 41 corresponds for the same reasons.

Howell's claims 42 and 44 specify a plurality of antibodies comprising a mixture of different antibodies or fragments thereof. Claim 26 of the present application specifies a mixture of antibodies. Since claim 26 of the present application corresponds to the proposed count for the reasons discussed above, Howell's claims 42 and 43 correspond for the same reasons.

Howell's claim 43 specifies that the at least one antibody is a polyclonal antibody preparation or fragments of a polyclonal antibody preparation. Claim 35 of the present application specifies polyclonal antibodies or fragments. Since claim 35 of the present application corresponds to the proposed count for the reasons discussed above, Howell's claim 43 corresponds for the same reasons.

37 CFR 41.202(a)(3)

Set forth below is a claim chart comparing applicant's claim 23 and Howell et al.'s claim 1 to the proposed count and showing why those claims interfere within the meaning of §41.203(a):

Claim 23 of the Present Application

23. A method of enhancing an immune response in a patient having soluble cytokine receptor molecules in the blood which inhibit the immune response, the method comprising:

(a) obtaining whole blood from the patient;

(b) separating plasma from the blood;

(c) contacting the plasma with at least one cytokine receptor inhibitor

Claim 1 of the Howell et al. Patent

1. A method of stimulating an immune response in a mammal having a pathological condition, comprising:

a. obtaining whole blood from the mammal;

b. separating the whole blood into a cellular component and an acellular component or a fraction of the acellular component, wherein said acellular component or said fraction of the acellular component contains a targeted immune system inhibitor selected from the group consisting of soluble receptors for tumor necrosis factors .alpha. and .beta., interleukin-1 receptor antagonist, soluble receptors for interferon-.gamma., soluble receptors for interleukin-1, and soluble receptors for interleukin-6;

c. contacting the acellular component or said fraction of the acellular

selected from the group consisting of antibodies or antibody fragments binding to soluble cytokine receptor molecules, and cytokine molecules and epitopes thereof binding to soluble cytokine receptor molecules;

(d) removing soluble cytokine receptor molecules bound to the cytokine receptor inhibitor from the plasma; and

(e) returning the plasma from which the soluble cytokine receptor molecules have been removed to the patient.

component with a binding partner capable of specifically binding to said targeted immune system inhibitor;

d. removing the binding partner bound to said targeted immune system inhibitor from said acellular component or said fraction of said acellular component to produce an altered acellular component or altered fraction of the acellular component having a reduced amount of the targeted immune system inhibitor;

e. combining the cellular component with the altered acellular component or altered fraction of the acellular component to produce altered whole blood; and

f. administering the altered whole blood to the mammal.

Claim 23 of the present application and Howell's claim 1 interfere because those claims are directed to the same patentable invention. Both claims are directed to "enhancing" (claim 23 of the present application) or "stimulating" (Howell's claim 1) an immune response.

Claim 23 of the present application specifies a patient as the subject while Howell's claim 1 specifies a mammal. This is not a patentable distinction because humans are mammals and are the subject of many therapeutic methods such as claimed here.

Steps (a) in each claim are substantially the same. Those steps specify obtaining whole blood from the subject.

Steps (b) of each claim are also substantially the same. Claim 23 of the present application specifies "separating the plasma from the blood." Howell's claim 1 accomplishes the same result in the end by separating an "acellular component" from the blood. Plasma is, in fact, the acellular component of whole blood.

Howell's step (b) specifies that acellular component contains a "targeted immune system inhibitor" selected from a specified group. Step (b) of claim 23 of the present application does not contain this recitation. Rather, the preamble of claim 23 specifies that the patient has "soluble cytokine receptor molecules in the blood which inhibit the immune response." Thus, the "soluble cytokine receptor molecules" specified in claim 23 of the present application is substantially the same as the "targeted immune system inhibitor" specified in Howell's claim 1. Accordingly, claim 23 of the present application is generic to Howell's claim 1 in this respect. The Markush grouping in claim 1 of the Howell et al. patent contains a significantly large number of species such that it is not patentably distinct from claim 23 of the present application.

Steps (c) of each claim specify contacting the plasma or acellular component with a "cytokine receptor inhibitor" (claim 1 of the present application) or "binding partner capable

of specifically binding to said targeted immune system inhibitor” (Howell’s claim 1). The function of these species is the same-- i.e., to form a complex between the soluble cytokine receptor molecules or targeted immune system inhibitor and the cytokine receptor inhibitor or the binding partner capable of specifically binding to the targeted immune system inhibitor.

Step (c) of claim 23 of the present application specifies a Markush grouping for the cytokine receptor inhibitor. Howell’s claim 1, in contrast, is generic with respect to this limitation. However, the grouping specified in claim 23 of the present application is sufficiently broad such that it is not patentably distinct from Howell’s claim 1.

Steps (d) of each claim are substantially the same. Each claim specifies removing the complex discussed above from the plasma or acellular component.

Howell’s claim 1 does specify in step (d) that the removal produces “an altered acellular component or altered fraction of the acellular component having a reduced amount of the targeted immune system inhibitor.” However, this merely states explicitly what is implicit in claim 23 of the present application. Based on applicant’s current understanding of the invention, this is the mechanism by which “enhancing an immune response in a patient” specified in the preamble of claim 23 is accomplished.

Step (e) of claim 23 of the present application is substantially the same as steps (e) and (f) of Howell’s claim 1. Step (e) of claim 23 specifies “returning the plasma from which the soluble cytokine receptor molecules have been removed to the patient.” Steps (e) and (f) of Howell’s claim 1 accomplishes the same result. The difference is that, in step (e) of Howell’s claim 1, the “altered acellular component” (or fraction) is combined with the cellular component to produce altered whole blood, and then that altered whole blood is administered to the mammal.

Combining the acellular and cellular components as specified in Howell’s claim 1 does not render that claim patentably distinct from claim 23 of the present application. It was

well-known in the relevant timeframe in the relevant field that treated plasma (i.e., an acellular component) can be combined with the cellular components of blood prior to administering such reconstituted whole blood to the subject. See the abstract and column 4, line 19-20 of Lentz U.S. patent No. 4,708,713, of record.

37 CFR 41.202(a)(4)

Applicant will likely prevail on priority because its effective filing date is prior to Howell's effective filing date. The present application is a continuation-in-part of U.S. application serial No. 09/699,003 (hereinafter referred to as "the '003 application"), filed on October 26, 2000. The '003 application is a continuation of U.S. application serial No. 09/316,226 (hereinafter referred to as "the '226 application"), filed on May 21, 1999. The '226 application is a continuation-in-part of U.S. application serial No. 09/083,307 (hereinafter referred to as "the '307 application"), filed on May 22, 1998. The present application also claims benefit of the filing date of U.S. provisional application serial No. 60/164,695 (hereinafter referred to as "the '695 application"), filed on November 10, 1999. As will be discussed in detail below, the '226, '307, and '695 applications each provides a construction reduction to practice of at least one embodiment within the scope of the count.

In contrast, the Howell et al. patent issued from U.S. application serial No. 09/444,144 (hereinafter referred to as "the '144 application"), which was filed on November 20, 1999. The '144 application does not claim benefit of the filing date of any earlier-filed application under 35 U.S.C. §§ 119 or 120.

Since the effective filing dates of applicant's '226, '307, and '695 applications are each prior to the November 20, 1999 filing date of Howell et al.'s '144 application, applicants will likely prevail on priority.

37 CFR 41.202(a)(5)

Set forth below is a claim chart showing the written description for claims 23-41 of the present application in the specification of that application.

<u>Claim</u>	<u>Specification</u>
23. A method of enhancing an immune response in a patient having soluble cytokine receptor molecules in the blood which inhibit the immune response, the method comprising:	Page 1, lines 6-7
(a) obtaining whole blood from the patient;	Page 18, lines 4-8
(b) separating plasma from the blood;	Page 18, lines 6-8.
(c) contacting the plasma with at least one cytokine receptor inhibitor selected from the group consisting of antibodies or antibody fragments binding to soluble cytokine receptor molecules, and cytokine molecules and epitopes thereof binding to soluble cytokine receptor molecules;	Page 6, lines 13-20; page 18, lines 8-11
(d) removing soluble cytokine receptor molecules bound to the cytokine	Page 6, lines 13-20; page 18, lines 8-18

receptor inhibitor from the plasma; and

(e) returning the plasma from
which the soluble cytokine receptor
molecules have been removed to the
patient.

Page 18, lines 12-15

24. The method of claim 23,
wherein the cytokine receptor inhibitor is
immobilized in a solid support or
membrane.

Page 6, line 15 and page 9, line 4

25. The method of claim 23,
wherein the antibodies are recombinant.

Page 6, lines 18-20

26. The method of claim 23,
wherein the antibodies are in a mixture of
antibodies immunoreactive with the
soluble cytokine receptor molecules.

Page 6, lines 14-18

27. The method of claim 23,
wherein the patient is human.

Page 6, line 26

28. The method of claim 23,
wherein the soluble cytokine receptor is
selected from the group consisting of
soluble receptors for tumor necrosis
factors alpha and beta.

Page 3, lines 14-17

29. The method of claim 23,
wherein the soluble cytokine receptor is

Page 6, lines 1-7 and page 9, line 19-20

selected from the group consisting of TNF
receptor, interleukin-1 receptor, and
interleukin-6 receptor.

30. The method of claim 23,
wherein the soluble cytokine receptor
molecule is a soluble interleukin-1
receptor or a soluble interleukin-6
receptor.

Page 6, lines 1-7

31. The method of claim 23,
wherein the soluble cytokine receptor
molecule is a TNF receptor.

Page 9, lines 19-20

32. The method of claim 23,
wherein the antibodies or antibody
fragments are monoclonal.

Page 6, line 27

33. The method of claim 23,
wherein the monoclonal antibodies or
antibody fragments are recombinant.

Page 6, lines 18-20

34. The method of claim 23,
wherein the plasma is contacted with
antibodies or antibody fragments.

Page 6, lines 18-20

35. The method of claim 23,
wherein the plasma is contacted with
polyclonal antibodies or antibody
fragments.

Page 6, line 27

36. The method of claim 23,
wherein the plasma is contacted with
monoclonal antibodies or antibody
fragments.

Page 6, line 27

37. The method of claim 23,
wherein the plasma is contacted with the
cytokines or cytokine epitopes.

Page 6, lines 13-14

38. The method of claim 36,
wherein the monoclonal antibodies or
antibody fragments are recombinant.

Page 6, lines 18-20

39. The method of claim 23,
wherein the blood is separated into plasma
by filtration.

Page 6, line 15; page 12, line 12 to page
13, line 2; and page 18, lines 4-8

40. The method of claim 39,
wherein the filtration is ultrafiltration.

Page 12, line 12 to page 13, line 2; and
page 18, lines 4-8

41. The method of claim 23,
wherein steps (a)-(e) are repeated.

Page 18, lines 21-24

37 CFR 41.202(a)(6)

Set forth below is a claim chart showing where applicant's disclosure in the present application provides a constructive reduction to practice within the scope of the interfering subject matter:

Claim

Reduction to Practice
in the Present Application

23. A method of enhancing an immune response in a patient having soluble cytokine receptor molecules in the blood which inhibit the immune response, the method comprising:

Page 1, lines 6-7

(a) obtaining whole blood from the patient;

Page 18, lines 4-8

(b) separating plasma from the blood;

Page 18, lines 6-8

(c) contacting the plasma with at least one cytokine receptor inhibitor selected from the group consisting of antibodies or antibody fragments binding to soluble cytokine receptor molecules, and cytokine molecules and epitopes thereof binding to soluble cytokine receptor molecules;

Page 6, lines 13-20; page 18, lines 8-11

(d) removing soluble cytokine receptor molecules bound to the cytokine receptor inhibitor from the plasma; and

Page 6, lines 13-20; page 18, lines 8-18

(e) returning the plasma from which the soluble cytokine receptor

Page 18, lines 12-15

molecules have been removed to the
patient.

As noted above, the present application is a continuation-in-part of the '003 application, filed October 26, 2000. Set forth below is a claim chart showing where the disclosure of the '003 application provides a constructive reduction to practice within the scope of the interfering subject matter:

Claim

Reduction to Practice
in the '003 Application

23. A method of enhancing an
immune response in a patient having
soluble cytokine receptor molecules in the
blood which inhibit the immune response,
the method comprising:

Page 1, lines 3-5

(a) obtaining whole blood from the
patient;

Page 6, lines 15-16

(b) separating plasma from the
blood;

Page 5, lines 16-22

(c) contacting the plasma with at
least one cytokine receptor inhibitor
selected from the group consisting of
antibodies or antibody fragments binding
to soluble cytokine receptor molecules,
and cytokine molecules and epitopes

Page 11, line 2 to page 12, line 16

thereof binding to soluble cytokine
receptor molecules;

(d) removing soluble cytokine

Page 12, line 7-16

receptor molecules bound to the cytokine
receptor inhibitor from the plasma; and

(e) returning the plasma from

Page 7, lines 5-7 and 23-25

which the soluble cytokine receptor
molecules have been removed to the
patient.

The '003 application is a continuation of the '226 application, filed May 21, 1999.
The specification of the '003 application and the '226 application are the same. Therefore,
the claim chart for the '003 application presented above also applies to the '226 application.

The '226 application is a continuation-in-part of the '307 application filed May 22,
1998. Set forth below is a claim chart showing where the disclosure of the '307 application
provides a constructive reduction to practice within the scope of the interfering subject
matter:

Claim

Reduction to Practice
in the '307 Application

23. A method of enhancing an
immune response in a patient having
soluble cytokine receptor molecules in the
blood which inhibit the immune response,
the method comprising:

Page 1, lines 3-4

- | | |
|--|--|
| (a) obtaining whole blood from the patient; | Page 6, lines 5-6 |
| (b) separating plasma from the blood; | Page 5, lines 12; page 6, lines 9-10; page 7, lines 6-11 |
| (c) contacting the plasma with at least one cytokine receptor inhibitor selected from the group consisting of antibodies or antibody fragments binding to soluble cytokine receptor molecules, and cytokine molecules and epitopes thereof binding to soluble cytokine receptor molecules; | Page 11, lines 2-26 |
| (d) removing soluble cytokine receptor molecules bound to the cytokine receptor inhibitor from the plasma; and | Page 11, lines 23-26 |
| (e) returning the plasma from which the soluble cytokine receptor molecules have been removed to the patient. | Page 6, lines 17-19; page 7, lines 14-16 |

The present application also claims benefit of the filing date of the '695 application. Set forth below is a claim chart showing where the disclosure of the '695 application provides a constructive reduction to practice within the scope of the interfering subject matter:

Claim

Reduction to Practice
in the '695 Application

23. A method of enhancing an immune response in a patient having soluble cytokine receptor molecules in the blood which inhibit the immune response, the method comprising:

Page 1, lines 5-8

(a) obtaining whole blood from the patient;

Page 10, lines 11-12; page 10, lines 11-12

(b) separating plasma from the blood;

Page 9, lines 16-17; page 10, lines 13-16;
page 11-16

(c) contacting the plasma with at least one cytokine receptor inhibitor selected from the group consisting of antibodies or antibody fragments binding to soluble cytokine receptor molecules, and cytokine molecules and epitopes thereof binding to soluble cytokine receptor molecules;

Page 3, lines 3-6; page 4, lines 4-20; page 18, last three lines

(d) removing soluble cytokine receptor molecules bound to the cytokine receptor inhibitor from the plasma; and

Page 3, lines 3-6; page 4, lines 4-7 and 19-20; page 18, last three lines

(e) returning the plasma from which the soluble cytokine receptor

Page 9, lines 16-17; page 11, lines 1-3 and 19-21; page 18, last three lines

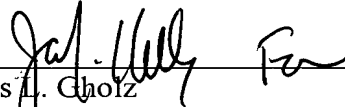
Application No. 09/709,045
Suggestion of an Interference

molecules have been removed to the
patient.

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Suggestion of an Interference

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